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TI Prucalopride is effective in patients with severe chronic constipation in whom laxatives fail to provide adequate relief. Results of a double-blind, placebo-controlled clinical trial.
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SO Digestion, (2003) Vol. 67, No. 1-2, pp. 82-9.
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CY Switzerland
DT (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS Priority Journals
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TI Prucalopride is effective in patients with severe chronic constipation in whom laxatives fail to provide adequate relief. Results of a double-blind, placebo-controlled clinical trial.
AB BACKGROUND: Chronic constipation (CC) is common and there is a need for more effective and better-tolerated agents that normalize bowel function without affecting secretion. Prucalopride is a novel, selective serotonin(4) receptor agonist with enterokinetic properties. AIMS: Pilot study to compare the efficacy and tolerability of prucalopride and placebo in patients with severe CC referred to a tertiary centre. METHODS: After 4-weeks' run in, patients were randomized to 4 weeks' once daily, double-blind treatment with either prucalopride 4 mg (n = 27) or placebo (n = 26). A 50% dose reduction after 2 weeks' treatment was possible for patients with an excessive gastrointestinal response to the study medication (severe cramps, abdominal pain, and diarrhea). Patients assessed efficacy using a visual analogue scale (VAS) and recorded bowel function in daily diaries. The investigator assessed efficacy and total gut transit time (marker study). RESULTS: Patient VAS assessment demonstrated that prucalopride was significantly more effective than placebo in softening stools, and decreasing straining and time to first stool. Prucalopride also had a positive effect on stool frequency, feeling of complete evacuation and total gut transit time, although these differences were not statistically significant compared with placebo. The most common adverse events were gastrointestinal symptoms and headache; most were mild to moderate. There were no clinically relevant effects on cardiovascular or laboratory parameters. CONCLUSIONS: Once-daily prucalopride 4 mg for 4 weeks is effective and well tolerated in patients with severe CC. It improves whole gut transit, reducing straining, softening stools and reducing time to first bowel movement.

CT Check Tags: Female; Male
Adult
*Benzofurans: TU, therapeutic use
*Cathartics: TU, therapeutic use
Chronic Disease
*Constipation: DT, drug therapy
Dose-Response Relationship, Drug
Double-Blind Method
Gastrointestinal Transit: DE, drug effects
Gastrointestinal Transit: PH, physiology
Humans

Middle Aged
Pilot Projects
Safety
Serotonin Antagonists: TU, therapeutic use
Severity of Illness Index

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TI New and emerging treatments for irritable bowel syndrome and functional dyspepsia.
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SO Expert opinion on emerging drugs, (2002 May) Vol. 7, No. 1, pp. 91-8.
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CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; PUBMED-NOT-MEDLINE
EM 200507
ED Entered STN: 2 Jul 2005
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AB The symptomatic management of irritable bowel syndrome (IBS) and functional dyspepsia, which often overlap, can be frustrating and difficult. Education and reassurance remain central for management although controlled trials are lacking. Psychological interventions may be useful in select patients but methodological inadequacies in clinical trials limit their interpretability. For symptom exacerbations, drug treatment is reasonable but no current treatment successfully targets the full symptom complex. Bulking agents are not of proven efficacy in IBS; they may improve constipation but worsen bloating and pain. Anticholinergics are of uncertain value in IBS . A meta-analysis of trials of smooth muscle relaxants for IBS has been reported to be positive but the quality of the trials included was poor. Antidepressants for IBS and functional dyspepsia appear to be efficacious based on the limited published evidence; both global symptoms and abdominal pain improve. Selective serotonin reuptake inhibitors (SSRIs) are of uncertain efficacy but anecdotally appear to be useful. Laxatives are not of proven efficacy in IBS. Loperamide improves diarrhea, but not abdominal pain in IBS. No drug is of proven efficacy for bloating. Acid suppression remains the mainstay of therapy for functional dyspepsia but the majority of patients do not have an adequate response. Promising drugs include new prokinetics for constipation-predominant IBS (e.g., tegaserod, a partial 5-HT4 agonist, prucalopride, a full 5-HT4 agonist, and dexloxiglumide, a cholecystokinin1 antagonist), agents for diarrhea-predominant IBS (e.g., 5-HT3 antagonists, alpha2 receptor agonists and corticotrophin receptor-1 antagonists), other visceral analgesics (e.g. tachykinin antagonists, opioid agonists) and in dyspepsia fundus relaxing agents (e.g., 5-HT1 agonists, tegaserod).

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TI Management of irritable bowel syndrome: novel approaches to the pharmacology of gut motility.
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SO Canadian journal of gastroenterology = Journal canadien de gastroenterologie, (1999 Mar) Vol. 13 Suppl A, pp. 50A-65A. Ref: 169
Journal code: 8807867. ISSN: 0835-7900.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 1 Jun 1999
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AB Although it is unclear to what extent irritable bowel syndrome (IBS) symptoms represent a normal perception of abnormal function or an abnormal perception of normal function, many believe that IBS constitutes the clinical expression of an underlying motility disorder, affecting primarily the mid- and lower gut. Indeed, transit and contractile abnormalities have been demonstrated with sophisticated techniques in a subset of patients with IBS. As a consequence, drugs affecting gastrointestinal (GI) motility have been widely employed with the aim of correcting the major IBS manifestations, ie, pain and altered bowel function. Unfortunately, no single drug has proven to be effective in treating IBS symptom complex. In addition, the use of some medications has often been associated with unpleasant side effects. Therefore, the search for a truly effective and safe drug to control motility disturbances in IBS continues. Several classes of drugs look promising and are under evaluation. Among the motor-inhibiting drugs, gut selective muscarinic antagonists (such as zamifenacin and darifenacin), neurokinin2 antagonists (such as MEN-10627 and MEN-11420), beta3-adrenoreceptor agonists (eg, SR-58611A) and GI-selective calcium channel blockers (eg, pinaverium bromide and octylonium) are able to decrease painful contractile activity in the gut (antispasmodic effect), without significantly affecting other body functions. Novel mechanisms to stimulate GI motility and transit include blockade of cholecystokinin (CCK)A receptors and stimulation of motilin receptors. Loxiglumide (and its dextroisomer, dexloxiglumide) is the only CCKA receptor antagonist that is being evaluated clinically. This drug accelerates gastric emptying and colonic transit, thereby increasing the number of bowel movements in patients with chronic constipation. It is also able to reduce visceral perception. Erythromycin and related 14-member macrolide compounds inhibit the binding of motilin to its receptors on GI smooth muscle and, therefore, act as motilin agonists. This antibiotic accelerates gastric emptying and shortens orocecal transit time. In the large bowel a significant decrease in transit is observed only in the right colon, which suggests a shift in fecal distribution. Several 'motilinomimetics' have been synthesized. Their development depends on the lack of antimicrobial activity and the absence of fading of the prokinetic effect during prolonged administration. 5-hydroxytryptamine (5-HT)4 agonists with significant pharmacological effects on the mid- and distal gut (such as prucalopride and tegaserod) are available for human use. These 'enterokinetic' compounds are useful for treating constipation-predominant IBS patients. 5-HT3 receptor antagonists also possess a number of interesting pharmacological properties that may make them suitable for treatment of IBS. Besides decreasing colonic sensitivity to distension, these drugs prolong

intestinal transit and may be particularly useful in diarrhea-predominant IBS. Finally, when administered in small pulsed doses, octreotide, besides reducing the perception of rectal distension, accelerates intestinal transit, although other evidence disputes such an effect.

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TI Effect of enterokinetic prucalopride on intestinal motility in fast rats.
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SO World journal of gastroenterology : WJG, (2003 Sep) Vol. 9, No. 9, pp. 2065-7.
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CY China
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LA English
FS Priority Journals
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TI Effect of enterokinetic prucalopride on intestinal motility in fast rats.
AB AIM: To evaluate the effects of prucalopride on intestinal prokinetic activity in fast rats and to provide experimental basis for clinical treatment of gastrointestinal motility diseases. METHODS: Gastrointestinal propulsion rate was measured by the migration rate of activated charcoal, which reflexes gastrointestinal motility function. 120 Spraque-Dawley rats were randomly divided into four groups and received an intravenous injection of physiological saline (served as control), prucalopride 1 mg/kg, prucalopride 2 mg/kg and cisapride 1 mg/kg, respectively. The gastrointestinal propulsion rate was measured 1, 2 or 4 hours after intravenous injection of the drugs. RESULTS: Significant accelerations of gastrointestinal propulsion rate in prucalopride 1 mg/kg and 2 mg/kg groups were found compared with control group at 2 and 4 hours(83.2 %+/-5.5 %, 81.7 %+/-8.5 % vs 70.5 %+/-9.2 %, P<0.01; 91.2 %+/-2.2 %, 91.3 %+/-3.9 % vs 86.8 %+/-2.6 %, P<0.01).The gastrointestinal propulsion rates at 1, 2 or 4 hours were faster in prucalopride 1 mg/kg and 2 mg/kg groups than in cisapride group (84.0 %+/-11.7 %, 77.1 %+/-11.9 % vs 66.3 %+/-13.6 %, P<0.01, P<0.05; 83.2 %+/-5.5 %, 81.7 %+/- 8.5 % vs 75.4 %+/-5.9 %, P<0.01, P<0.05; 91.2 %+/-2.2 %, 91.3 %+/-3.9 % vs 88.6 %+/-3.5 %,P<0.05, P<0.05). No difference of gastrointestinal propulsion rate was found between prucalopride 1 mg/kg group and prucalopride 2 mg/kg group (P>0.05). CONCLUSION: Prucalopride accelerates intestinal motility in fast rats, and has no dose dependent effect.
CT Check Tags: Male
Animals
*Benzofurans: PD, pharmacology
*Fasting: PH, physiology
*Gastrointestinal Motility: DE, drug effects
Rats
Rats, Sprague-Dawley
Receptors, Serotonin: DE, drug effects
Receptors, Serotonin, 5-HT4
*Serotonin Agonists: PD, pharmacology
Time Factors